

## GENOMIC METHYLATION OF PERIPHERAL BLOOD LEUKOCYTES AMONG ARSENIC-EXPOSED MATERNAL-NEWBORN PAIRS

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**Background and Aims:** An emerging body of evidence indicates that early-life arsenic (As) exposure may influence the trajectory of health outcomes later in life; however, the mechanisms underlying these observations are unknown. Our previous work indicates that chronic As exposure causes epigenetic dysregulation, including increases in DNA methylation in adults. The objective of this study was to investigate the influence of prenatal As exposure on genomic methylation of cord blood DNA in a study of mother/newborn pairs in Bangladesh.

**Methods:** Maternal and cord blood DNA was available from a convenience sample of 101 mother/newborn pairs. Measures of As exposure included maternal urinary As (uAs), maternal blood As (mbAs) and cord blood As (cbAs). Several measures of genomic DNA methylation were assessed, including the [3H]-methyl-incorporation assay and three Pyrosequencing assays; Alu, LINE-1 and LUMA.

**Results:** After adjustment for covariates, increasing quartiles of maternal uAs were positively associated with cord blood genomic DNA methylation as measured by the [3H]-methyl-incorporation assay ( $p_{\text{trend}} < 0.05$ ), and LINE-1 methylation (Q1 vs. Q3;  $p=0.03$ ), indicating that newborn DNA methylation increased with maternal As exposure. The effects appear to be gender specific: among male newborns ( $N=58$ ), mbAs was associated with increased DNA methylation as measured by Alu ( $r=0.28$ ;  $p=0.03$ ), LINE-1 ( $r=0.23$ ;  $p<0.1$ ) and [3H]-methyl-incorporation ( $r=-0.22$ ;  $p<0.1$ ). Among female newborns ( $N=42$ ), the correlations between maternal uAs and cbAs and Alu and Line-1, while not significant, were negative ( $r=-0.24$ ;  $p=0.12$ ) and ( $r=-0.18$ ;  $p=0.24$ ), respectively.

**Conclusions:** Consistent with our previous studies in adults, these results suggests that prenatal As exposure is associated with increases in genomic DNA methylation in newborn cord blood DNA. Although the sample size is small, the data suggest that this may occur in a gender-specific manner. Arsenic-induced epigenetic modifications *in utero* may potentially influence disease outcomes later in life.